Notice of Allowability	Application No.	Applicant(s)	
	09/996,507	WANG, LAIXIN	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *10/24/05*.

2. ☒ The allowed claim(s) is/are *1,5-16,19-22,27,30,31,36-41,44-48,50-52,56-64,84-88,95 and 96*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Donna Fugit on 1/3/06.

The application has been amended as follows:

IN THE SPECIFICATION:

Delete the paragraph bridging pages 11 and 12 and replace with the following:

--The carrier molecule may also include at least one lysis agent connected to the biocompatible hydrophilic backbone or to a bound polycationic polymer. The lysis agent could be any membrane fusion peptide or protein. The lysis agent can be selected to break down a biological membrane such as a cell, endosomal, or nuclear membrane, thereby allowing the polyanionic macromolecule to be released into the cytoplasm or nucleus of the cell. As a result of the presence of the lysis agent, the membrane undergoes lysis, fusion, or both. Such lysis agents may include a viral peptide, a bacterial toxin, a lytic peptide, ~~aleveolysin,~~ alveolysin, bifermentolysin, ~~boutulinolysin~~, botulinolysin, ~~capriciolysin,~~ cereolysin O, chauveolysin, histolyticolysin O, pneumolysin, ~~sealigerolysin,~~ seeligerolysin, septicolysin O, sordellilysin, ~~streptoslysin O,~~ streptolysin O, ~~tenaolysin~~ tenolysin or thuringolysin O, and active fragments thereof. A lytic peptide is a chemical grouping which penetrates a membrane such that the structural

organization and integrity of the membrane is lost. Lysis agents also include viruses and synthetic compounds that can break down a biological membrane. Fragments of the above listed lysis agents which will provide endosomal escape activity may also be employed in the present invention. Other peptides and proteins are known to cause the breakdown or fusion ~~of~~ of biological membranes and maybe used as a lysis agent within the scope of the invention. Jahn, R. & Sudhof T., *Annu. Rev. Biochem.* **68**: 863-911 (1999). Pecheur, E.I., et al, *J Membrane Biol.* **167**: 1-17 (1999).--

IN THE CLAIMS:

8. (currently amended) The carrier of claim 7, wherein the at least one lysis agent is selected from the group consisting of a viral peptide, a bacterial toxin, a lytic peptide, ~~aleveolysin,~~ alveolysin, bifermentolysin, ~~boutulinolysin~~, botulinolysin, ~~capriciolysin,~~ cereolysin O, chauveolysin, histolyticolysin O, pneumolysin, ~~sealigerolysin,~~ seeligerolysin, septicolysin O, sordellilysin, ~~streptoslysin O,~~ streptolysin O, ~~tenaolysin~~ tenolysin or thuringolysin O, and active fragments thereof.

In claim 16, delete "abaout" and substitute --about-- therefor.

In claim 27, delete "22" and substitute --1-- therefor.

In claim 31, delete "HPMA" and substitute --poly (N-(2-hydroxypropyl)methacrylamide) (HPMA)-- therefor.

37. (currently amended) The complex of claim 31, wherein the nucleic acid is selected from the group consisting of an antisense oligonucleotide, a ribozyme, a DNAzyme, a chimeric RNA/DNA, a phosphorothioate oligonucleotide, a 2'-O-methyl oligonucleotide, a DNA-PNA conjugate, a DNA-morpholino-DNA conjugate, and a combination thereof.

45. (currently amended) The complex of claim 31, further comprising at least one lysis agent connected to the HPMA backbone polymer or to one of the two or more PEI polymers, the at least one lysis agent selected from the group consisting of a viral peptide, a bacterial toxin, a lytic peptide, ~~aleveolysin,~~ alveolysin, bifermentolysin, ~~boutulinolysin~~, botulinolysin, ~~capriciolysin,~~ cereolysin O, chauveolysin, histolyticolysin O, pneumolysin, ~~sealigerolysin,~~ seeligerolysin, septicolysin O, sordellilysin, ~~streptoslysin O,~~ streptolysin O, ~~tenaolysin~~ tenolysin or thuringolysin O, and active fragments thereof.

48. (currently amended) A method of transporting a polyanionic macromolecule across a membrane of a cell comprising:

(a) complexing the polyanionic macromolecule to a carrier molecule to create a

complex, the carrier molecule consisting of a single biocompatible hydrophilic backbone polymer and two or more polycationic polymers covalently linked to the biocompatible hydrophilic backbone polymer by ~~a~~ biodegradable peptide linkers which ~~is~~ are from about 2 to about 100 atoms in length, wherein the biocompatible hydrophilic backbone polymer is selected from the group consisting of PEG and HPMA; and

(b) contacting the cell with the complex.

Cancel claim 49.

52. (currently amended) The method of claim 48, further comprising at least one lysis agent connected to the biocompatible hydrophilic backbone polymer or to one of the two or more polycationic polymers, the at least one lysis agent selected from the group consisting of a viral peptide, a bacterial toxin, a lytic peptide, ~~aleveolysin,~~ alveolysin, bifermentolysin, ~~boutulinolysin~~, botulinolysin, ~~capriciolysin,~~ cereolysin O, chauveolysin, histolyticolysin O, pneumolysin, ~~sealigerolysin,~~ seeligerolysin, septicolysin O, sordellilysin, ~~streptoslysin O,~~ streptolysin O, ~~tenaolysin~~ tenolysin or thuringolysin O, and active fragments thereof.

In claims 63 and 64 delete "linker" and substitute --linkers-- therefor.

In claim 95, delete "linker is" and substitute --linkers are-- therefor.

Conclusion

Amendments to claims 8,16, 37, 45, 52, 63, 64, and 95 correct obvious typographical or grammatical errors. Applicant agreed to delete "capriciolysin" from the specification and claims because neither the Examiner nor Applicant could determine its meaning. The scope of claim 48 was narrowed to include the limitations of cancelled claim 49 in order to overcome potential art rejections over methods of transfecting cells with DNA/polycationic polypeptide complexes.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635

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(FILE 'HOME' ENTERED AT 16:53:45 ON 28 DEC 2005)

FILE 'MEDLINE' ENTERED AT 16:53:52 ON 28 DEC 2005
L1 1 SEA PLU=ON (AKIYAMA Y?/AU OR VINGRADOV S?/AU) AND COPOLYMER
D BIB AB
L2 17 SEA PLU=ON (AKIYAMA Y?/AU OR VINOGRADOV S?/AU) AND COPOLYMER
D TI 1-17
D BIB AB 12
L3 758 SEA PLU=ON AKIYAMA Y?/AU
L4 1 SEA PLU=ON L3 AND PEI
D BIB AB
L5 5 SEA PLU=ON L3 AND PEG
D BIB AB 1-5

FILE 'MEDLINE' ENTERED AT 17:27:58 ON 28 DEC 2005
L6 0 SEA PLU=ON HYDROPHILIC POLYMER AND POLYCATION AND LINKER
L7 81 SEA PLU=ON (POLYETHYLENEGLYCOL OR POLY ETHYLENEGLYCOL OR POLY
ETHYLENE GLYCOL OR POLYETHYLENE GLYCOL) AND POLYCATION?
D TI 40-81
L8 41 SEA PLU=ON L7 AND (TRANSFEC? OR PLASMID OR DNA OR VECTOR)
D TI 1-41
D BIB AB 39 37 36 34 23 17 16 13 12

FILE 'STNGUIDE' ENTERED AT 17:34:39 ON 28 DEC 2005

FILE 'MEDLINE' ENTERED AT 17:48:55 ON 28 DEC 2005
L9 219 SEA PLU=ON POLY N-2-HYDROXYPROPYL METHACRYLAMIDE OR ?HYDROXYPR
OPYLMETHACRYLAMIDE OR POLYHYDROXYPROPYLMETHACRYLAMIDE OR
?HYDROXYPROPYL METHACRYLAMIDE OR POLY HYDROXYPROPYLMETHACRYLAMI
DE OR POLY HYDROXYPROPYL METHACRYLAMIDE
L10 7 SEA PLU=ON L9 AND POLYCATION
L11 7 SEA PLU=ON L9 AND POLYCATION?
D BIB AB 1-7

FILE 'STNGUIDE' ENTERED AT 17:54:07 ON 28 DEC 2005

FILE 'CAPLUS, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH' ENTERED AT 17:55:11
ON 28 DEC 2005
L12 248 SEA PLU=ON L8 OR L11
L13 145 DUP REM L12 (103 DUPLICATES REMOVED)
D TI 100-145
D BIB AB 101 102 109 112 113 120 128 130 144 145

FILE 'STNGUIDE' ENTERED AT 18:01:00 ON 28 DEC 2005

FILE 'MEDLINE, CAPLUS' ENTERED AT 18:05:54 ON 28 DEC 2005
L14 2 SEA PLU=ON STAR SHAPED AND COPOLYMERS ENHANCE DNA CONDENSATION

D BIB AB 1

FILE 'STNGUIDE' ENTERED AT 18:07:57 ON 28 DEC 2005

FILE 'MEDLINE, CAPLUS' ENTERED AT 18:13:54 ON 28 DEC 2005
D TI 80-100

FILE 'STNGUIDE' ENTERED AT 18:13:59 ON 28 DEC 2005

FILE 'CAPLUS, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH' ENTERED AT 18:14:12
ON 28 DEC 2005
D TI L13 80-99

FILE 'STNGUIDE' ENTERED AT 18:14:15 ON 28 DEC 2005

FILE 'MEDLINE, CAPLUS' ENTERED AT 18:16:06 ON 28 DEC 2005
D BIB AB 95 81

FILE 'STNGUIDE' ENTERED AT 18:16:11 ON 28 DEC 2005

FILE 'CAPLUS, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH' ENTERED AT 18:16:20
ON 28 DEC 2005
D BIB AB L13 81 95

FILE 'STNGUIDE' ENTERED AT 18:16:22 ON 28 DEC 2005

FILE HOME

(FILE 'HOME' ENTERED AT 06:15:28 ON 29 DEC 2005)

FILE 'MEDLINE' ENTERED AT 06:15:34 ON 29 DEC 2005
L1 0 SEA PLU=ON ALEVEOLYSIN
L2 28 SEA PLU=ON ALVEOLYSIN

FILE 'STNGUIDE' ENTERED AT 06:16:02 ON 29 DEC 2005

FILE 'MEDLINE' ENTERED AT 06:20:35 ON 29 DEC 2005
L3 0 SEA PLU=ON SEALIGEROLYSIN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
AQUASCI, BIOENG, BIOSIS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB,
CIN, CONFSCI, CROPB, CROPU, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2,
DRUGU, EMBAL, EMBASE, ESBIOBASE, FEDRIP, ...' ENTERED AT 06:21:01 ON 29
DEC 2005
L4 8 SEA PLU=ON L3
L5 5 DUP REM L4 (3 DUPLICATES REMOVED)
D KWIC 1-5
D BIB ABD 1-5
D BIB 1-5

FILE 'STNGUIDE' ENTERED AT 06:23:18 ON 29 DEC 2005

FILE 'MEDLINE' ENTERED AT 06:25:43 ON 29 DEC 2005
L6 0 SEA PLU=ON STREPTOSLYSIN OR TENAOLYSIN
L7 2342 SEA PLU=ON STREPTOLYSIN
L8 0 SEA PLU=ON CAPRICIOLYSIN
L9 0 SEA PLU=ON CAPRICOLYSIN
L10 0 SEA PLU=ON CAPRIOLYSIN
L11 0 SEA PLU=ON CAPREOLYSIN

FILE 'STNGUIDE' ENTERED AT 06:37:24 ON 29 DEC 2005

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,

AQUASCI, BIOENG, BIOSIS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB,
CIN, CONFSCI, CROPB, CROPU, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2,
DRUGU, EMBAL, EMBASE, ESBIOBASE, FEDRIP, ...' ENTERED AT 06:40:15 ON 29
DEC 2005
L12 8 SEA PLU=ON CAPRICIOLYSIN
L13 5 DUP REM L12 (3 DUPLICATES REMOVED)
D BIB AB KWIC 1-5